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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,030	09/12/2006	Gianluca Gazza	82062-0169	6978

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HOGAN & HARTSON LLP
IP GROUP, COLUMBIA SQUARE
555 THIRTEENTH STREET, N.W.
WASHINGTON, DC 20004

EXAMINER	
BERRIOS, JENNIFER A	

ART UNIT	PAPER NUMBER
4121	

NOTIFICATION DATE	DELIVERY MODE
03/04/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

dcptopatent@hhlaw.com
rogruwell@hhlaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,030	GAZZA, GIANLUCA	
	Examiner	Art Unit	
	Jennifer A. Berrios	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/16/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *33-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/3/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-42 are currently pending.

Election/Restriction

1. Applicant's election of Group I in the reply filed on 1/16/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Examiner would like to address the typographical errors pointed out by the Applicant and confirm that claims 4-32 are indeed part of Group I.

3. Claims 33-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups II and III, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 1/16/2009.

Priority

This application is a 371 of PCT application PCT/IB03/01958, filed May 22, 2003 and claims benefit of priority of PCT application PCT/IB03/01232, filed April 4, 2003.

Acknowledgement is made of applicant's claim for foreign priority based on the application filed on May 22, 2003 and April 4, 2003. Claims 1-32 will receive the priority date of April 4, 2003.

Claim Rejections – 35 USC § 112 – 2nd Paragraph

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 17-19 recites the limitation "active ingredient" in while reading upon claim 1, which has no mention of an active ingredient limitation. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections – 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-9, and 16-20 rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,027,741 (issued" 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6, 579,978 (filed: 4/3/1998).

5. Claims 1-3 teach a stent comprising a coating of a ester derivative of hyaluronic acid (HA) polymer, in which the ester derivative has all or some carboxyl groups selected from the aliphatic, aryalipathic, and other; more specifically from the benzyl alcohol series. Claims 4-7 further limit claim 1 by defining the degree of esterification of the hyaluronic acid ester derivative which varies from 50-100%, 70-100%, 100% and

75% of the carboxyl groups of the HA. Claims 8-9 further limit claim 1 by teaching that the stent has a pharmacologically active ingredient associated with the HA polymer coating, the active ingredient selected from an anti-inflammatory, anti-proliferative, anti-migratory and an immunosuppressant. Claims 16-19 teach that the stent comprising an active ingredient and HA are released from the HA polymer coating, with the coating have a thickness of .5-40 microns, preferably of 5-10 microns, over a prolonged period of time, or after one month and within 2 weeks. Claim 20 teaches the stent of claim 1 comprising a layer of HA bound to the stent and a coating of HA polymer.

6. The '741 patent teaches a coated biomedical object or device having a coating of sulfated polysaccharide, wherein the polysaccharide is a hyaluronic acid, hyaluronate ester or a salt thereof, Specifically a sulfated hyaluronate ester (column 16, claims 1 and 4). The '741 patent further teaches that important derivatives of hyaluronic acid are esters thereof with alcohol of the aliphatic, araliphatic, heterocyclic and cycloalipathic series (Column 2, Lines 35-45). US '741 further explain examples of sulfated hyaluronic acid ester that can be used in the present invention. Examples of such include HYAFF 11 (meaning 100% of the carboxyl groups are in the form of benzyl esters) (Column 4, lines 38-43); HYAFF 11p75 (75% benzyl ester of HA) (Column 7, lines 55-58).

7. US '741 also teaches that pharmaceutical preparations and biomaterials comprising sulfated derivatives of HA can be administered alone or in association with other chemical polymers and/or pharmacologically acceptable drugs (column 14, example 16). Examples include the association of a sulfated HA and a HA ester with an

antibiotic, anti-inflammatory, antimicrobial, antibacterial and more (Column 15, lines 15-20).

8. The '741 patent fails to teach what constitutes a biomedical object or device. The '978 patent teaches biomaterials comprising sulphated hyaluronic acid compounds and derivatives thereof (Claim 1 and 13), wherein the derivative is selected from the group consisting of a partial or total ester (claim 14). The biomaterials can be used to advantage in various fields of surgery, such as in the preparation of cardiac valves and vascular stents (column 5, lines 66-67-column 6, lines 4-5).

9. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to combine the teaching of the '741 and the '978 patent. One of ordinary skill in the art would have been motivated to substitute a stent for a biomedical object, because it was well known at the time of the invention that stents comprising sulphonated hyaluronic acid compounds and derivatives thereof, are advantages in various fields of surgery, as these compounds have anticoagulant and antithrombotic activities (see Abs. of Patent '978)

10. The '741 patent also fails to teach the time period for the release of the HA and the active ingredient from the HA polymer coating. As the stent described in the instant claim 1 comprises the same coating and HA as the biomedical device of the '741 patent it is expected that the properties of the devices be the same. Therefore the device of the '741 patent would have the same expectancy of release as the stent of instant claim 1.

11. The above mentioned prior art also fails to teach the thickness of the polymer coating. Since the above art teaches the stent of instant claim 1, it would be obvious to one of ordinary skill to determine the optimum thickness of the HA polymer coating, that would be the most effective.

12. Therefore Claims 1-9 and 16-20 are rejected under 35 USC 103(a) as being unpatentable over the prior art.

13. Claims 11-14 and 17-19 are rejected under 35 USC 103(a) as being unpatentable over US patent 6,027,741 (issued" 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6, 579,978 (filed: 4/3/1998), as applied to claims 1-9 and 16-20 above, further in view of US 2002/0082679 (filing date: 11/1/2001)

14. US patents '741 and '978 teach the limitation of instant claims 11-14 and 17-19, however they fail to teach the further limitations of each set of claims. Instant claims 11-14 further limit the teachings of the stent of instant claim 1 comprising an active ingredient associated with the HA polymer coating in the quantity between .001mg and 10mg for the following actions: anti-inflammatory, anti-migratory, anti-proliferative and immunosuppressant. While, Claims 17-19 further teach that the stent comprising an active ingredient and HA are released from the HA polymer coating, over a prolonged period of time, or after one month and within 2 weeks. US 2002/0082679 provides a luminal prosthesis, such as vascular stents and grafts for reducing or inhibiting restenosis (Paragraph 0003). The luminal prosthesis allows for the programmed and

controlled substance delivery of therapeutic agents (Paragraph 0028). Therapeutic agents may be selected from a group consisting of immunosuppressants, anti-inflammatory, anti-proliferatives, and anti-migratory agents, among others (Paragraph 0029). It also teaches that the source of the therapeutic agent is a polymeric material including therapeutic capable moieties as a structural subunit of the polymer (Paragraph 0031). The prosthesis incorporates the substance by coating the substance on the prosthesis (Pg 21, claim 15). The total amount of the therapeutic agent is generally from .1 micrograms to 10g, but is preferably .1 micrograms to 10mg. This therapeutic agent may be released in a time period, as measured from the time of implanting the device, ranging from 1-200 days, 1-45days and 7-21 days.

15. US 2002/0082679 fails to teach the properties of luminal prosthesis to be those of the stent of the instant claims. However, the '741 patent, as applied to claims 1-9 and 16-20 above does teach the properties of the medical device.

16. It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the polymer and therapeutic coating as taught in US 2002/0082679 for the HA polymer coating and active agent taught in the '741 patent. One of ordinary skill in the art would be motivated to substitute two equivalents, in this case polymers, which are taught by the prior art to be useful for the same purpose. Finally, a person of skill in the art would reasonably have expected to be successful because both references disclose biomedical objects comprising a polymer coating that contain an active therapeutic agent.

17. Claims 20-23, 25-26 and 28-32 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued" 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6, 579,978 (filed: 4/3/1998) and US 2002/0082679, as applied to claims 1-9, 11-14 and 16-20 above, (filing date: 11/1/2001) and further in view of US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005.

18. The US patents '741 and '978 teach the limitations of claims 20-23, 25-26 and 28-32, however fail to teach further limitations set forth by each set of claims.

19. Claims 21-23 and 32 further teach the stent of instant claim 1, further comprising a second coating of a polymer of hydrophobic nature, having a contact angle with water greater than 60°, applied directly to the surface of the stent. Claim 25 further specifies that the polymer of hydrophobic nature is polystyrene. Claims 26, 28 - 30 explain that the hydrophobic polymer, with a thickness of .5-40 micron, preferably 5-10 microns, is associated with an active ingredient (anti-inflammatory, anti-proliferative, anti-migratory and/or immunosuppressant). Said active ingredient is available in quantities between .0001mg and 10mg, and is released over a period of one month. Claim 31 teaches that the active coating of the two polymer coatings can be the same or different.

20. The '741 patent fails to teach whether the coated vascular stents contain one or more coating and the degree of contact with water for the hydrophobic polymer.

21. The '956 patent teaches a process for coating objects, for surgical, diagnostic and healthcare fields, with HA and derivatives thereof (see abstract). The '959 patent (column 14, example 11) takes a sample of polystyrene (hydrophobic polymer) from a bacteriological grade Petri dish and treats it with plasma. This treated sample is then

dipped and extracted from the following solutions: 1% HA acid; 1%HA and 1% 3-aminopropyltrimethoxy silane plus others; 1% HA 50% esterified with benzyl alcohol and 3-aminopropyltrimethoxy silane plus others. The contact degree with water of polystyrene although not specifically stated can be expected to have the same properties as disclosed by the applicant since the polymers are equivalents to one another.

22. The above mentioned prior art also fails to teach the thickness of the polymer coating. Since the above art teaches the stent of instant claim 1 with the limitations of claim 21, it would've been *prima facie* obvious to one of ordinary skill at the time the invention was made to determine the optimum thickness of the HA polymer coating, that would be the most effective.

23. US 2002/0082679 teaches polymeric material on a stent containing therapeutic agents. US '741 teaches a stent with HA polymer coating which can additionally contain active agents and the '956 patent teaches an object coated with polymeric material (polystyrene) and HA polymer coating, although no mention of therapeutic agents are made. However as taught above in US 2002/0082679 the source of the therapeutic agents associated with vascular stent coatings are polymers.

24. One of ordinary skill in the art at the time the invention was made would have been motivated to combine the teaching of US 2002/0082679, the '741 patent and the '956 patent since both the '741 patent and the '956 patent teaches stents coated with polymers and the '741 patent teaches that these polymers could contain therapeutic agents. It would be obvious to one of ordinary skill, as these two compositions are

taught by the prior art to be useful for the same purpose and therefore it would be obvious to combine the two to form a third composition for the same purpose.

25. Claim 24 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued" 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6, 579,978 (filed: 4/3/1998) and US 2002/0082679 (filing date: 11/1/2001) and US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005, as applied to claims 1-9, 11-14 ,16-23, 25-26 and 28-32 above,, and further in view of Vercruysse (Critical Reviews in Therapeutic Drug Carrier Systems, 1998).

26. The US patents '741, '978 and '959 teach the limitations of claim 24, however they fail to teach a the further limitation set forth by the claim. Claim 24 further teaches the second coating of the stent of instant claim 21 to be polymethyl methacrylate among others, with a contact degree angle with water of 60°. The above teachings fail to specify one of the exact polymers given in claim 24. The above art teaches a polystyrene coated with HA and derivates there of, while Vercruysse specifically teaches polymethyl methacrylate coated with HA (pg 528, lines 5-9).

27. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute polystyrene for polymethyl methacryalte since the prior art teaches these to be equivalents, both hydrophobic and both are coated with HA. The contact degree with water of polystyrene although not specifically stated can

be expected to have the same properties as disclosed by the applicant since the polymers can be considered equivalents to one another.

28. Claims 10 and 15 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued" 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6, 579,978 (filed: 4/3/1998) and US 2002/0082679, as applied to claims 1-9, 11-14 and 16-20 above, (filing date: 11/1/2001) and further in view of WO 99/03854 (pub date: 1/28/1999, cited on the 10/3/2005 IDS.

29. The US patents '741 and '978 and the '679 publication teach the limitations of claims 10 and 15, however fail to teach further limitations set forth by each claim. Claims 10 and 15 further teach that the active agent associated with the stent of instant claim one is specifically 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

30. US 2002/0082679 and the '741 patent teach the stent of instant claim 1 with an active agent, with quantities preferably of .1 micrograms to 10mg. What they fail to teach is the active ingredient being 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

31. WO 99/03854 teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl]

benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

32. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of WO 99/03854 with US 2002/0082679, the '741 patent and the '978 patent as it was well known at the time of the invention the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis.

33. Claim 27 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, in view of US patent 6, 579,978 (filed: 4/3/1998) and US 2002/0082679 (filing date: 11/1/2001) and US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005, as applied to claims 1, 6-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of WO 99/03854 (pub date: 1/28/1999).

34. The US patents '741 and '978 and '956 and the '679 publication teach the limitations of claim 27, however fail to teach the further limitations set forth the claim. Claim 27 further teaches that the active agent associated with the stent of instant claim 21 is specifically 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

35. The above teaching fails to teach this exact active ingredient as the therapeutic agent. WO 99/03854 teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-

(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

36. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US patents '741 and '978 and '956 and the '679 publication with WO 99/03854 as it was well known at the time of the invention the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berríos whose telephone number is (571)270-7679. The examiner can normally be reached on M-F 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

J.B.

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4121